

10540421

## Connecting via Winsock to STN

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LOGINID: ssspta1612bxr

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,  
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS      STN Operating Hours Plus Help Desk Availability

10540421

NEWS LOGIN      Welcome Banner and News Items  
NEWS IPC8      For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 22:11:52 ON 11 MAR 2008

=> file reg  
COST IN U.S. DOLLARS  
SINCE FILE ENTRY  
SESSION  
0.21  
0.21

FILE 'REGISTRY' ENTERED AT 22:11:58 ON 11 MAR 2008  
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STRUCTURE FILE UPDATES: 10 MAR 2008 HIGHEST RN 1007341-18-5  
DICTIONARY FILE UPDATES: 10 MAR 2008 HIGHEST RN 1007341-18-5

New CAS Information Use Policies, enter HELP USAGE TERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stnqgen/stndoc/properties.html>

```
=>
Uploading C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\asdgk.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1      STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
```

10540421

Structure attributes must be viewed using STN Express query preparation.

```
=> s 11
SAMPLE SEARCH INITIATED 22:14:41 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 303 TO ITERATE

100.0% PROCESSED 303 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01
```

```
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 5016 TO 7104
PROJECTED ANSWERS: 0 TO 0
```

L2 0 SEA SSS SAM L1

```
=> s 11 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 177.90 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 22:14:45 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 6538 TO ITERATE
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100.0% PROCESSED 6538 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01
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L3 2 SEA SSS FUL L1

```
=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
                           ENTRY SESSION
FULL ESTIMATED COST           180.20 180.41
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```
FILE 'HCAPLUS' ENTERED AT 22:14:49 ON 11 MAR 2008
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```

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FILE COVERS 1907 - 11 Mar 2008 VOL 148 ISS 11
FILE LAST UPDATED: 10 Mar 2008 (20080310/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

10540421

=> s 13  
L4 2 L3

=> s 14 and shinya, y?/au  
58 SHINYA, Y?/AU  
L5 0 L4 AND SHINYA, Y?/AU

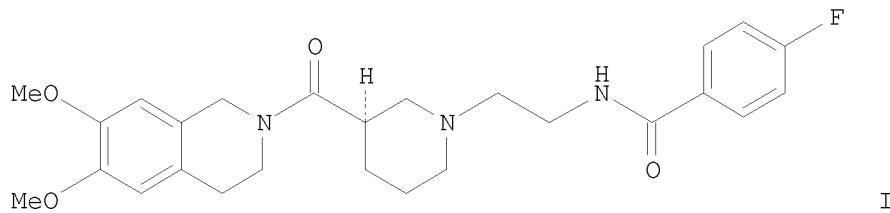
=> s 14 and watanabe, t?/au  
22474 WATANABE, T?/AU  
L6 2 L4 AND WATANABE, T?/AU

=> d 16, ibib abs hitstr, 1-2

L6 ANSWER 1 OF 2 HCPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2004:872791 HCPLUS  
DOCUMENT NUMBER: 141:350046  
TITLE: Preparation of novel crystal of fluorobenzamide derivative  
INVENTOR(S): Yoshida, Shinya; Watanabe, Toshihiro;  
Marumo, Kiyotaka; Yamaguchi, Sou  
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 25 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089933	A1	20041021	WO 2004-JP4794	20040401
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2519882	A1	20041021	CA 2004-2519882	20040401
EP 1609788	A1	20051228	EP 2004-725182	20040401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1771245	A	20060510	CN 2004-80009451	20040401
IN 2005DN04378	A	20070105	IN 2005-DN4378	20050927
MX 2005PA10603	A	20060725	MX 2005-PA10603	20050930
US 2007129357	A1	20070607	US 2005-552019	20051003
PRIORITY APPLN. INFO.:			JP 2003-99411	A 20030402
			WO 2004-JP4794	W 20040401

OTHER SOURCE(S): CASREACT 141:350046  
GI



AB A novel crystal of (R)-(-)-N-[2-[3-[(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl)carbonyl]piperidino]ethyl]-4-fluorobenzamide (I) monophosphate, which is known as a preventive and/or remedy for ischemic diseases such as angina pectoris and myocardial infarction and cardiovascular diseases such as ischemic heart failure and arrhythmia, was prepared and characterized by X-ray diffraction spectra and DSC. Two crystal forms ( $\alpha$  and  $\beta$  crystal forms) of compound I were prepared.  $\alpha$  Crystal form of compound I exhibited excellent moisture adsorption property and is advantageous for handling and formulation. Thus, 206.4 g (R)-1-[2-[(4-fluorobenzoyl)amino]ethyl]piperidine-3-carboxylic acid was treated with 810 mL DMF and 120.8 g 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline monohydrochloride, stirred, cooled, treated with 53.22 g Et<sub>3</sub>N at  $\leq 12^\circ$ , treated with 217 mL DMF and then successively with 21.32 g 1H-1,2,3-benzotriazole and 121.0 g 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride at  $\leq 5^\circ$ , and stirred at 0-4° for 15.5 h, and treated with 340 mL H<sub>2</sub>O, 2,000 mL EtOAc, and 550 mL 8% (W/V) aqueous NaOH solution to give, after workup and concentration, crude free base I (83.9% purity). I (11.90 g) was dissolved in ethanol to a total weight of 97.8 g, treated with 5 mL ethanol, 0.47 g H<sub>2</sub>O, and 0.86 g 85% H<sub>3</sub>PO<sub>4</sub>, and then with 5 mL ethanol, stirred at 30° overnight, and filtered to give, after washing the crystals with ethanol and drying, 3.38 g I monophosphate ( $\alpha$  crystal form).

IT 721452-52-4P, (R)-1-[2-[(4-Fluorobenzoyl)amino]ethyl]piperidine-3-carboxylic acid ethyl ester 721452-55-7P, (R)-1-[2-[(4-Fluorobenzoyl)amino]ethyl]piperidine-3-carboxylic acid  
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of novel crystal of fluorobenzamide monophosphate derivative having

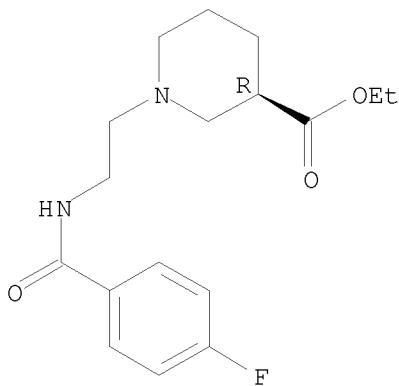
excellent moisture adsorption property)

RN 721452-52-4 HCPLUS

CN 3-Piperidinecarboxylic acid, 1-[2-[(4-fluorobenzoyl)amino]ethyl]-, ethyl ester, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

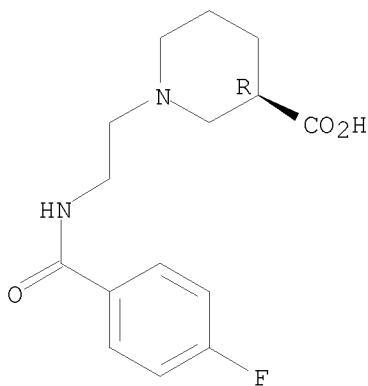
10540421



RN 721452-55-7 HCAPLUS

CN 3-Piperidinecarboxylic acid, 1-[2-[(4-fluorobenzoyl)amino]ethyl]-, (3R)-  
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:565208 HCAPLUS

DOCUMENT NUMBER: 141:106387

TITLE: Isoquinoline derivatives containing benzamide moiety  
and process for their preparation

INVENTOR(S): Yoshida, Shinya; Watanabe, Toshihiro;  
Marumo, Kiyotaka; Kakefuda, Akio

PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058710	A1	20040715	WO 2003-JP16582	20031224
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2511989	A1	20040715	CA 2003-2511989	20031224
AU 2003292757	A1	20040722	AU 2003-292757	20031224
CN 1753870	A	20060329	CN 2003-80109919	20031224
IN 2005DN02787	A	20070105	IN 2005-DN2787	20050623
US 2006084807	A1	20060420	US 2005-540421	20050624
KR 758522	B1	20070914	KR 2005-711965	20050624
PRIORITY APPLN. INFO.:			JP 2002-375153	A 20021225
			WO 2003-JP16582	W 20031224
OTHER SOURCE(S):	MARPAT 141:106387			
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

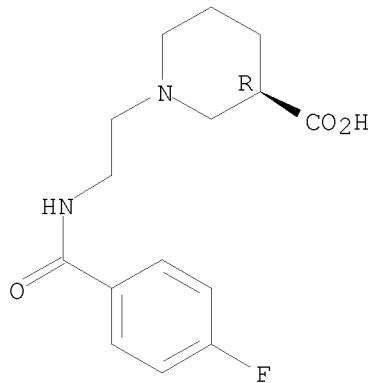
AB Process for the preparation of compds. I [R3 =, R4 = H, alkyl, alkoxy; Ar = (un)substituted aryl] and compds. II [R1 = H, alkyl, benzyl; R2 = H, protecting group of amino; Ar = (un)substituted aryl] were provided. For example, a mixture of compound (R)-II [R1 = Ethyl; R2 = H; Ar = 4-fluorophenyl] (37.94 g), e.g., prepared from (R)-piperidine-3-carboxylic acid Et ester L-tartaric acid salt in 4 steps, and 1 M aqueous NaOH (177 mL) in EtOH (100 mL) stirred at room temperature for 1 h. After treating the reaction with HCl to acidic pH, the solvent was azeotropically removed by toluene. Then, to a solution of the resulting residue in DMF (250 mL) were added 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (21.66 g), HOBT (7.97 g) and WSC hydrochloride (27.14 g) at 10 °C. The reaction was stirred at room temperature for 3 h, aqueous work-up followed by treatment with 85% phosphoric acid (13.65 g) in EtOH (500 mL) afforded claimed compound III phosphoric acid salt (44.25 g). Of note, compds. I are useful for prophylaxis and/or treatment of myocardial infarction, congestive heart failure, etc. (no data). The disclosed process employs less hazardous solvent.

IT 721452-55-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (N-benzoylaminoethylation of nipecotic acid derivs. using dihydrooxazoles)

RN 721452-55-7 HCPLUS  
 CN 3-Piperidinecarboxylic acid, 1-[2-[(4-fluorobenzoyl)amino]ethyl]-, (3R)- (CA INDEX NAME)

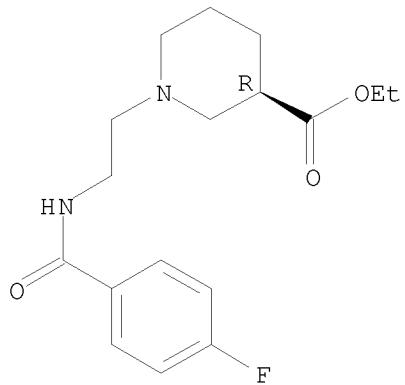
Absolute stereochemistry.

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IT 721452-52-4P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of isoquinoline derivs. via N-fluorobenzoylation of tetrahydroisoquinoline derivs.)  
RN 721452-52-4 HCAPLUS  
CN 3-Piperidinecarboxylic acid, 1-[2-[(4-fluorobenzoyl)amino]ethyl]-, ethyl ester, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



=> file caold		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	13.59	194.00
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-1.60	-1.60

FILE 'CAOLD' ENTERED AT 22:15:22 ON 11 MAR 2008

Updated Search

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FILE COVERS 1907-1966  
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d his

(FILE 'HOME' ENTERED AT 22:11:52 ON 11 MAR 2008)

FILE 'REGISTRY' ENTERED AT 22:11:58 ON 11 MAR 2008

L1                   STRUCTURE UPLOADED  
L2                   0 S L1  
L3                   2 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 22:14:49 ON 11 MAR 2008

L4                   2 S L3  
L5                   0 S L4 AND SHINYA, Y?/AU  
L6                   2 S L4 AND WATANABE, T?/AU

FILE 'CAOLD' ENTERED AT 22:15:22 ON 11 MAR 2008

=> s 13  
L7                   0 L3

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.46	194.46
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.60

FILE 'REGISTRY' ENTERED AT 22:15:28 ON 11 MAR 2008  
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STRUCTURE FILE UPDATES: 10 MAR 2008 HIGHEST RN 1007341-18-5  
DICTIONARY FILE UPDATES: 10 MAR 2008 HIGHEST RN 1007341-18-5

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>  
Uploading C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\421.str

L8 STRUCTURE UPLOADED

=> d 18  
L8 HAS NO ANSWERS  
L8 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s 18  
SAMPLE SEARCH INITIATED 22:16:48 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 309 TO ITERATE  
  
100.0% PROCESSED 309 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.01  
  
FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 5126 TO 7234  
PROJECTED ANSWERS: 0 TO 0

L9 0 SEA SSS SAM L8

=> s 18 full  
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 177.90 U.S. DOLLARS  
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y  
FULL SEARCH INITIATED 22:16:53 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 6564 TO ITERATE

100.0% PROCESSED 6564 ITERATIONS 9 ANSWERS  
SEARCH TIME: 00.00.01

L10 9 SEA SSS FUL L8

Updated Search

10540421

=> d his

(FILE 'HOME' ENTERED AT 22:11:52 ON 11 MAR 2008)

FILE 'REGISTRY' ENTERED AT 22:11:58 ON 11 MAR 2008

L1                   STRUCTURE UPLOADED  
L2                   0 S L1  
L3                   2 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 22:14:49 ON 11 MAR 2008

L4                   2 S L3  
L5                   0 S L4 AND SHINYA, Y?/AU  
L6                   2 S L4 AND WATANABE, T?/AU

FILE 'CAOLD' ENTERED AT 22:15:22 ON 11 MAR 2008

L7                   0 S L3

FILE 'REGISTRY' ENTERED AT 22:15:28 ON 11 MAR 2008

L8                   STRUCTURE UPLOADED  
L9                   0 S L8  
L10                  9 S L8 FULL

=> s l10 not 16

NUMERIC VALUE NOT VALID 'WATANABE, T?'  
                          0 WATANABE, T?/AU  
L11                  9 L10 NOT L6

=> file hcplus

	SINCE FILE ENTRY	TOTAL SESSION
COST IN U.S. DOLLARS		
FULL ESTIMATED COST	184.43	378.89
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.60

FILE 'HCAPLUS' ENTERED AT 22:17:15 ON 11 MAR 2008

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FILE COVERS 1907 - 11 Mar 2008 VOL 148 ISS 11  
FILE LAST UPDATED: 10 Mar 2008 (20080310/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

Updated Search

10540421

This file contains CAS Registry Numbers for easy and accurate substance identification.

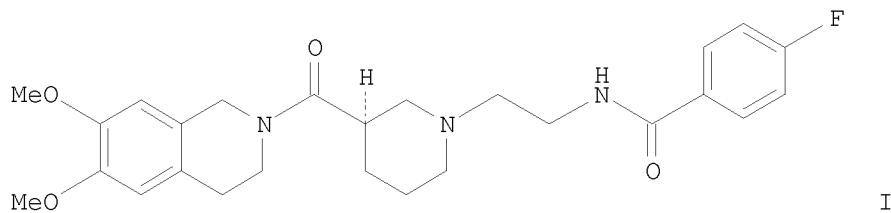
=> s 111  
L12 6 L11

=> s 112 and yoshida, s?/au  
9851 YOSHIDA, S?/AU  
L13 2 L12 AND YOSHIDA, S?/AU

=> d 113, ibib abs hitstr, 1-6

L13 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2004:872791 HCAPLUS  
DOCUMENT NUMBER: 141:350046  
TITLE: Preparation of novel crystal of fluorobenzamide derivative  
INVENTOR(S): Yoshida, Shinya; Watanabe, Toshihiro;  
Marumo, Kiyotaka; Yamaguchi, Sou  
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 25 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089933	A1	20041021	WO 2004-JP4794	20040401
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2519882	A1	20041021	CA 2004-2519882	20040401
EP 1609788	A1	20051228	EP 2004-725182	20040401
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IN 2005DN04378	A	20070105	IN 2005-DN4378	20050927
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US 2007129357	A1	20070607	US 2005-552019	20051003
PRIORITY APPLN. INFO.:			JP 2003-99411	A 20030402
			WO 2004-JP4794	W 20040401
OTHER SOURCE(S):	CASREACT	141:350046		
GI				



AB A novel crystal of (R)-(-)-N-[2-[3-[(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl)carbonyl]piperidino]ethyl]-4-fluorobenzamide (I) monophosphate, which is known as a preventive and/or remedy for ischemic diseases such as angina pectoris and myocardial infarction and cardiovascular diseases such as ischemic heart failure and arrhythmia, was prepared and characterized by X-ray diffraction spectra and DSC. Two crystal forms ( $\alpha$  and  $\beta$  crystal forms) of compound I were prepared.  $\alpha$  Crystal form of compound I exhibited excellent moisture adsorption property and is advantageous for handling and formulation. Thus, 206.4 g (R)-1-[2-[(4-fluorobenzoyl)amino]ethyl]piperidine-3-carboxylic acid was treated with 810 mL DMF and 120.8 g 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline monohydrochloride, stirred, cooled, treated with 53.22 g Et<sub>3</sub>N at  $\leq 12^\circ$ , treated with 217 mL DMF and then successively with 21.32 g 1H-1,2,3-benzotriazole and 121.0 g 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride at  $\leq 5^\circ$ , and stirred at 0-4° for 15.5 h, and treated with 340 mL H<sub>2</sub>O, 2,000 mL EtOAc, and 550 mL 8% (W/V) aqueous NaOH solution to give, after workup and concentration, crude free base I (83.9% purity). I (11.90 g) was dissolved in ethanol to a total weight of 97.8 g, treated with 5 mL ethanol, 0.47 g H<sub>2</sub>O, and 0.86 g 85% H<sub>3</sub>PO<sub>4</sub>, and then with 5 mL ethanol, stirred at 30° overnight, and filtered to give, after washing the crystals with ethanol and drying, 3.38 g I monophosphate ( $\alpha$  crystal form).

IT 721452-52-4P, (R)-1-[2-[(4-Fluorobenzoyl)amino]ethyl]piperidine-3-carboxylic acid ethyl ester 721452-55-7P, (R)-1-[2-[(4-Fluorobenzoyl)amino]ethyl]piperidine-3-carboxylic acid  
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

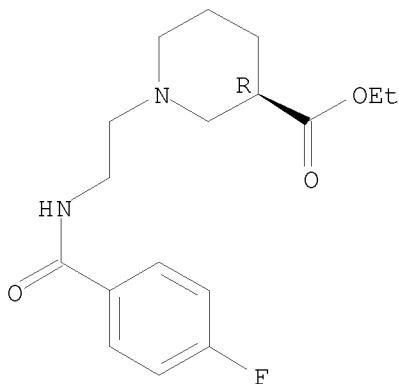
(preparation of novel crystal of fluorobenzamide monophosphate derivative having

excellent moisture adsorption property)

RN 721452-52-4 HCAPLUS

CN 3-Piperidinecarboxylic acid, 1-[2-[(4-fluorobenzoyl)amino]ethyl]-, ethyl ester, (3R)- (CA INDEX NAME)

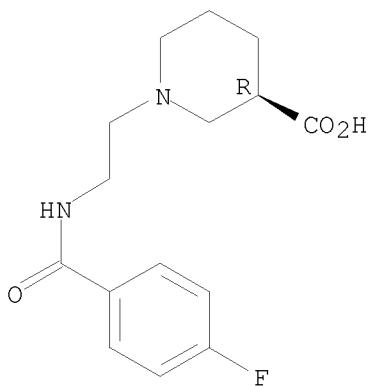
Absolute stereochemistry.



RN 721452-55-7 HCPLUS

CN 3-Piperidinecarboxylic acid, 1-[2-[(4-fluorobenzoyl)amino]ethyl]-, (3R)-  
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 2 HCPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:565208 HCPLUS

DOCUMENT NUMBER: 141:106387

TITLE: Isoquinoline derivatives containing benzamide moiety and process for their preparation

INVENTOR(S): Yoshida, Shinya; Watanabe, Toshihiro;

Marumo, Kiyotaka; Kakefuda, Akio

PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058710	A1	20040715	WO 2003-JP16582	20031224
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2511989	A1	20040715	CA 2003-2511989	20031224
AU 2003292757	A1	20040722	AU 2003-292757	20031224
CN 1753870	A	20060329	CN 2003-80109919	20031224
IN 2005DN02787	A	20070105	IN 2005-DN2787	20050623
US 2006084807	A1	20060420	US 2005-540421	20050624
KR 758522	B1	20070914	KR 2005-711965	20050624
PRIORITY APPLN. INFO.:			JP 2002-375153	A 20021225
			WO 2003-JP16582	W 20031224
OTHER SOURCE(S):	MARPAT 141:106387			
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

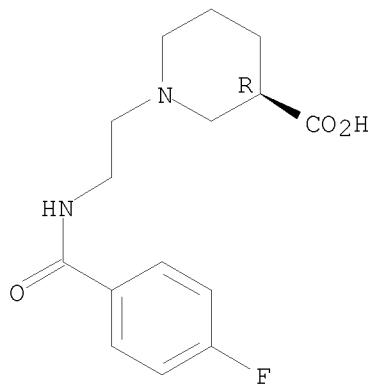
AB Process for the preparation of compds. I [R3 =, R4 = H, alkyl, alkoxy; Ar = (un)substituted aryl] and compds. II [R1 = H, alkyl, benzyl; R2 = H, protecting group of amino; Ar = (un)substituted aryl] were provided. For example, a mixture of compound (R)-II [R1 = Ethyl; R2 = H; Ar = 4-fluorophenyl] (37.94 g), e.g., prepared from (R)-piperidine-3-carboxylic acid Et ester L-tartaric acid salt in 4 steps, and 1 M aqueous NaOH (177 mL) in EtOH (100 mL) stirred at room temperature for 1 h. After treating the reaction with HCl to acidic pH, the solvent was azeotropically removed by toluene. Then, to a solution of the resulting residue in DMF (250 mL) were added 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (21.66 g), HOBT (7.97 g) and WSC hydrochloride (27.14 g) at 10 °C. The reaction was stirred at room temperature for 3 h, aqueous work-up followed by treatment with 85% phosphoric acid (13.65 g) in EtOH (500 mL) afforded claimed compound III phosphoric acid salt (44.25 g). Of note, compds. I are useful for prophylaxis and/or treatment of myocardial infarction, congestive heart failure, etc. (no data). The disclosed process employs less hazardous solvent.

IT 721452-55-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (N-benzoylaminoethylation of nipecotic acid derivs. using dihydrooxazoles)

RN 721452-55-7 HCPLUS  
 CN 3-Piperidinecarboxylic acid, 1-[2-[(4-fluorobenzoyl)amino]ethyl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

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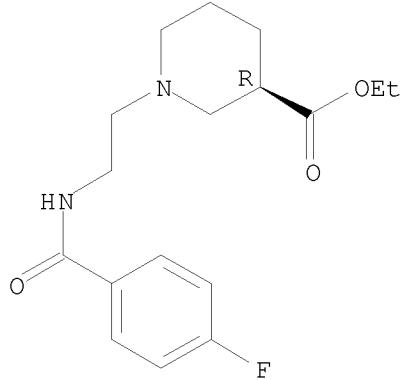
IT 721452-52-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of isoquinoline derivs. via N-fluorobenzoylation of tetrahydroisoquinoline derivs.)

RN 721452-52-4 HCAPLUS

CN 3-Piperidinecarboxylic acid, 1-[2-[(4-fluorobenzoyl)amino]ethyl]-, ethyl ester, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



=> d his

(FILE 'HOME' ENTERED AT 22:11:52 ON 11 MAR 2008)

FILE 'REGISTRY' ENTERED AT 22:11:58 ON 11 MAR 2008

L1 STRUCTURE uploaded

L2 0 S L1

L3 2 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 22:14:49 ON 11 MAR 2008

Updated Search

10540421

L4 2 S L3  
L5 0 S L4 AND SHINYA, Y?/AU  
L6 2 S L4 AND WATANABE, T?/AU

FILE 'CAOLD' ENTERED AT 22:15:22 ON 11 MAR 2008  
L7 0 S L3

FILE 'REGISTRY' ENTERED AT 22:15:28 ON 11 MAR 2008  
L8 STRUCTURE UPLOADED  
L9 0 S L8  
L10 9 S L8 FULL  
L11 9 S L10 NOT L6

FILE 'HCAPLUS' ENTERED AT 22:17:15 ON 11 MAR 2008  
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L13 2 S L12 AND YOSHIDA, S?/AU

=> s l12 not l13  
L14 4 L12 NOT L13

=> s l14 and watanabe, t?/au  
22474 WATANABE, T?/AU  
L15 0 L14 AND WATANABE, T?/AU

=> s l14 and marumo, k?/au  
217 MARUMO, K?/AU  
L16 0 L14 AND MARUMO, K?/AU

=> s l14 and kakefuda, a?/au  
45 KAKEFUDA, A?/AU  
L17 0 L14 AND KAKEFUDA, A?/AU

=> s l11/uses  
6 L11  
6920858 USES/RL  
L18 2 L11/USES  
(L11 (L) USES/RL)

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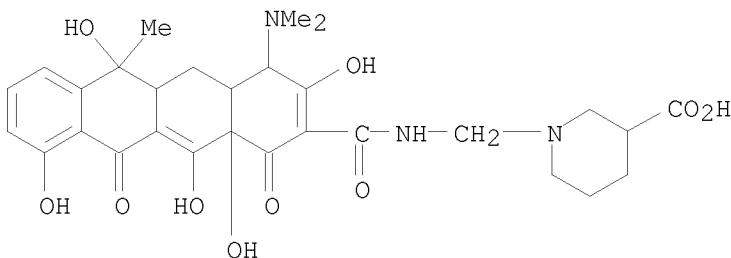
L18 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2006:405003 HCAPLUS  
DOCUMENT NUMBER: 146:155278  
TITLE: Non-stochastic and stochastic linear indices of the  
molecular pseudograph's atom-adjacency matrix: a novel  
approach for computational in silico screening and  
"rational" selection of new lead antibacterial agents  
AUTHOR(S): Marrero-Ponce, Yovani; Marrero, Ricardo Medina;  
Torrens, Francisco; Martinez, Yamile; Bernal, Milagros  
Garcia; Zaldivar, Vicente Romero; Castro, Eduardo A.;  
Abalo, Ricardo Grau  
CORPORATE SOURCE: Department of Pharmacy, Faculty of Chemical-Pharmacy,  
Central University of Las Villas, Santa Clara, 54830,  
Cuba  
SOURCE: Journal of Molecular Modeling (2006), 12(3), 255-271  
CODEN: JMMOFK; ISSN: 0948-5023

URL: <http://www.springerlink.com/media/ef6tmfk36j3ttmb97w1h/contributions/1/2/v/4/12v47qr26320v870.pdf>

PUBLISHER: Springer GmbH  
 DOCUMENT TYPE: Journal; (online computer file)  
 LANGUAGE: English

AB A novel approach (TOMOCOMD-CARDD) to computer-aided rational drug design is illustrated. This approach is based on the calcn. of the non-stochastic and stochastic linear indexes of the mol. pseudograph's atom-adjacency matrix representing mol. structures. These TOMOCOMD-CARDD descriptors are introduced for the computational (virtual) screening and rational selection of new lead antibacterial agents using linear discrimination anal. The two structure-based antibacterial-activity classification models, including non-stochastic and stochastic indexes, classify correctly 91.61% and 90.75%, resp., of 1525 chems. in training sets. These models show high Matthews correlation coeffs. (MCC = 0.84 and 0.82). An external validation process was carried out to assess the robustness and predictive power of the model obtained. These QSAR models permit the correct classification of 91.49% and 89.31% of 505 compds. in an external test set, yielding MCCs of 0.84 and 0.79, resp. The TOMOCOMD-CARDD approach compares satisfactorily with respect to nine of the most useful models for antimicrobial selection reported to date. Finally, an in silico screening of 87 new chems. reported in the antiinfective field with antibacterial activities is developed showing the ability of the TOMOCOMD-CARDD models to identify new lead antibacterial compds.

IT 15301-82-3, Pecocycline  
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (novel QSAR model TOMOCOMD-CARDD in computer-aided rational drug design for selection of new lead antibacterial agents using linear discrimination anal.)  
 RN 15301-82-3 HCAPLUS  
 CN 3-Piperidinecarboxylic acid, (4S,4aS,5aS,6S,12aS)-1-[[[4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenyl]carbonyl]amino]methyl]- (CA INDEX NAME)



REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:244333 HCAPLUS  
 DOCUMENT NUMBER: 143:307  
 TITLE: Atom, atom-type, and total nonstochastic and stochastic quadratic fingerprints: a promising

AUTHOR(S): approach for modeling of antibacterial activity  
 Marrero-Ponce, Yovani; Medina-Marrero, Ricardo;  
 Torrens, Francisco; Martinez, Yamile; Romero-Zaldivar,  
 Vicente; Castro, Eduardo A.

CORPORATE SOURCE: Department of Pharmacy, Faculty of Chemical-Pharmacy,  
 Central University of Las Villas, Santa Clara, 54830,  
 Cuba

SOURCE: Bioorganic & Medicinal Chemistry (2005), 13(8),  
 2881-2899

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The Topol. Mol. Computer Design (TOMOCOMD-CARDD) approach has been introduced for the classification and design of antimicrobial agents using computer-aided mol. design. For this propose, atom, atom-type, and total quadratic indexes have been generalized to codify chemical structure information. In this sense, stochastic quadratic indexes have been introduced for the description of the mol. structure. These stochastic fingerprints are based on a simple model for the intramol. movement of all valence-bond electrons. In this work, a complete data set containing 1006 antimicrobial agents is collected and presented. Two structure-based antibacterial activity classification models have been generated. The models (including nonstochastic and stochastic indexes) classify correctly more than 90% of 1525 compds. in training sets. These models permit the correct classification of 92.28% and 89.31% of 505 compds. in an external test sets. The approach, also, satisfactorily compares with respect to nine of the most useful models for antimicrobial selection reported to date. Finally, a virtual screening of 87 new compds. reported in the anti-infective field with antibacterial activities is developed showing the ability of the models to identify new leads as antibacterial.

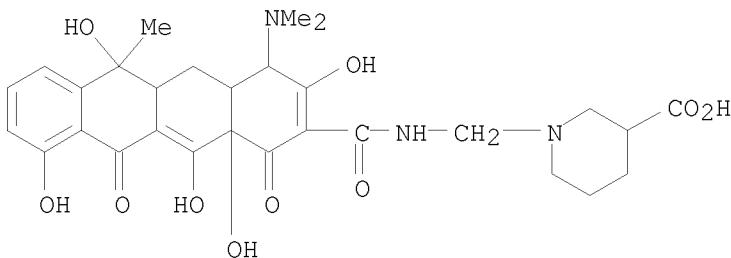
IT 15301-82-3, Pecocycline

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(atom, atom-type, and total nonstochastic and stochastic quadratic fingerprints as promising approach for modeling antibacterial activity)

RN 15301-82-3 HCPLUS

CN 3-Piperidinecarboxylic acid, (4S,4aS,5aS,6S,12aS)-1-[[[4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenyl]carbonyl]amino]methyl]- (CA INDEX NAME)



REFERENCE COUNT:

91

THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10540421

=> d his

(FILE 'HOME' ENTERED AT 22:11:52 ON 11 MAR 2008)

FILE 'REGISTRY' ENTERED AT 22:11:58 ON 11 MAR 2008

L1 STRUCTURE UPLOADED  
L2 0 S L1  
L3 2 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 22:14:49 ON 11 MAR 2008

L4 2 S L3  
L5 0 S L4 AND SHINYA, Y?/AU  
L6 2 S L4 AND WATANABE, T?/AU

FILE 'CAOLD' ENTERED AT 22:15:22 ON 11 MAR 2008

L7 0 S L3

FILE 'REGISTRY' ENTERED AT 22:15:28 ON 11 MAR 2008

L8 STRUCTURE UPLOADED  
L9 0 S L8  
L10 9 S L8 FULL  
L11 9 S L10 NOT L6

FILE 'HCAPLUS' ENTERED AT 22:17:15 ON 11 MAR 2008

L12 6 S L11  
L13 2 S L12 AND YOSHIDA, S?/AU  
L14 4 S L12 NOT L13  
L15 0 S L14 AND WATANABE, T?/AU  
L16 0 S L14 AND MARUMO, K?/AU  
L17 0 S L14 AND KAKEFUDA, A?/AU  
L18 2 S L11/USES

=> file caold

	SINCE FILE ENTRY	TOTAL SESSION
COST IN U.S. DOLLARS		
FULL ESTIMATED COST	29.87	408.76
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.20	-4.80

FILE 'CAOLD' ENTERED AT 22:18:56 ON 11 MAR 2008

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FILE COVERS 1907-1966

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> s l11  
L19 1 L11

=> d l19, all, 1

L19 ANSWER 1 OF 1 CAOLD COPYRIGHT 2008 ACS on STN

AN CA63:13180h CAOLD

TI pyrenylmethylamines

AU Clarke, Robert LaGrone; Buck, J. S.

PA Sterling Drug Inc.

DT Patent

PATENT NO. KIND DATE

PI	US 3198835	1965				
IT	897-41-6	1729-05-1	3590-94-1	3590-95-2	3590-96-3	3591-02-4
	3590-97-4	3590-98-5	3590-99-6	3591-00-2	3591-01-3	3591-02-4
	3591-03-5	3712-78-5	3712-79-6	3765-68-2	3786-54-7	3786-55-8
	3786-56-9	3786-57-0	3786-59-2	3786-60-5	3786-61-6	3786-62-7
	3786-63-8	3786-66-1	3786-67-2	3804-54-4	3804-55-5	3806-02-8
	3840-95-7	3874-63-3	4914-39-0	6614-22-8	101201-45-0	
	104298-70-6	106439-18-3				

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.61	410.37
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-4.80

FILE 'REGISTRY' ENTERED AT 22:19:57 ON 11 MAR 2008  
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STRUCTURE FILE UPDATES: 10 MAR 2008 HIGHEST RN 1007341-18-5  
DICTIONARY FILE UPDATES: 10 MAR 2008 HIGHEST RN 1007341-18-5

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when

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conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=> S 6614-22-8/RN

L20 1 6614-22-8/RN

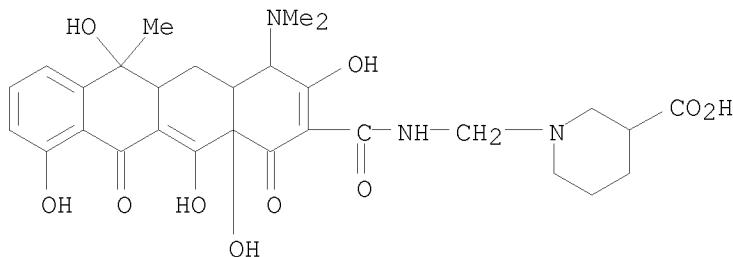
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NOTICE SET TO 1 U.S. DOLLAR FOR DISPLAY COMMAND  
SET COMMAND COMPLETED

=> D L20 SQIDE 1-

YOU HAVE REQUESTED DATA FROM 1 ANSWERS - CONTINUE? Y/(N):y  
THE ESTIMATED COST FOR THIS REQUEST IS 6.65 U.S. DOLLARS  
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L20 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN  
RN 6614-22-8 REGISTRY  
CN Nipecotic acid, 1-[(4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamido)methyl]-, hydrochloride (7CI, 8CI) (CA INDEX NAME)  
MF C29 H35 N3 O10 . Cl H  
LC STN Files: CA, CAOLD, CAPLUS, USPATOLD  
DT.CA CAplus document type: Patent  
RL.P Roles from patents: PREP (Preparation)  
CRN (741608-18-4)



● HCl

2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

10540421

=> SET NOTICE LOGIN DISPLAY

NOTICE SET TO OFF FOR DISPLAY COMMAND  
SET COMMAND COMPLETED

⇒

FILE 'REGISTRY' ENTERED AT 22:20:39 ON 11 MAR 2008  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 MAR 2008 HIGHEST RN 1007341-18-5  
DICTIONARY FILE UPDATES: 10 MAR 2008 HIGHEST RN 1007341-18-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>  
Uploading C:\Documents and Settings\brobinson1\My Documents\stnweb\Queries\2ef.str

L21 STRUCTURE UPLOADED

=> d 121  
L21 HAS NO ANSWERS  
L21 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s 121

10540421

SAMPLE SEARCH INITIATED 22:21:53 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 8538 TO ITERATE

23.4% PROCESSED 2000 ITERATIONS 0 ANSWERS  
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 165221 TO 176299  
PROJECTED ANSWERS: 0 TO 0

L22 0 SEA SSS SAM L21

=> s l21 full  
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 177.90 U.S. DOLLARS  
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y  
FULL SEARCH INITIATED 22:21:57 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 170590 TO ITERATE

100.0% PROCESSED 170590 ITERATIONS 3 ANSWERS  
SEARCH TIME: 00.00.03

L23 3 SEA SSS FUL L21

=> d his

(FILE 'HOME' ENTERED AT 22:11:52 ON 11 MAR 2008)  
FILE 'REGISTRY' ENTERED AT 22:11:58 ON 11 MAR 2008  
L1 STRUCTURE uploaded  
L2 0 S L1  
L3 2 S L1 FULL  
  
FILE 'HCAPLUS' ENTERED AT 22:14:49 ON 11 MAR 2008  
L4 2 S L3  
L5 0 S L4 AND SHINYA, Y?/AU  
L6 2 S L4 AND WATANABE, T?/AU  
  
FILE 'CAOLD' ENTERED AT 22:15:22 ON 11 MAR 2008  
L7 0 S L3  
  
FILE 'REGISTRY' ENTERED AT 22:15:28 ON 11 MAR 2008  
L8 STRUCTURE uploaded  
L9 0 S L8  
L10 9 S L8 FULL  
L11 9 S L10 NOT L6  
  
FILE 'HCAPLUS' ENTERED AT 22:17:15 ON 11 MAR 2008  
L12 6 S L11  
L13 2 S L12 AND YOSHIDA, S?/AU  
L14 4 S L12 NOT L13  
L15 0 S L14 AND WATANABE, T?/AU  
L16 0 S L14 AND MARUMO, K?/AU  
L17 0 S L14 AND KAKEFUDA, A?/AU  
L18 2 S L11/USES

10540421

FILE 'CAOLD' ENTERED AT 22:18:56 ON 11 MAR 2008  
L19 1 S L11

FILE 'REGISTRY' ENTERED AT 22:19:57 ON 11 MAR 2008  
L20 1 S 6614-22-8/RN  
SET NOTICE 1 DISPLAY  
SET NOTICE LOGIN DISPLAY

FILE 'REGISTRY' ENTERED AT 22:20:39 ON 11 MAR 2008  
L21 STRUCTURE UPLOADED  
L22 0 S L21  
L23 3 S L21 FULL

=> s l23 not l3  
L24 1 L23 NOT L3

=> s l24 not l11  
L25 1 L24 NOT L11

=> s l24 not l18  
'USES' IS NOT A VALID CROSSOVER QUALIFIER FOR L11  
Answer sets created in a different file may be field qualified with a  
limited set of qualifiers. Enter HELP CROSSOVER at an arrow prompt  
(=>) for specific information.

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	179.28	592.11
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-4.80

FILE 'HCAPLUS' ENTERED AT 22:22:31 ON 11 MAR 2008  
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FILE COVERS 1907 - 11 Mar 2008 VOL 148 ISS 11  
FILE LAST UPDATED: 10 Mar 2008 (20080310/ED)

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10540421

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L26 2 L25

=> s 126 and yoshida, s?/au  
9851 YOSHIDA, S?/AU  
L27 0 L26 AND YOSHIDA, S?/AU

=> s 126 and watanabe, t?/au  
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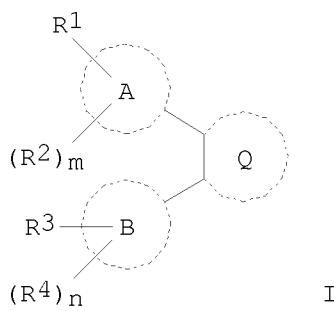
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L29 0 L26 AND MARUMO, K?/AU

=> s 126 and kakefuda, a?/au  
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L30 0 L26 AND KAKEFUDA, A?/AU

=> d 126, ibib abs hitstr, 1-2

L26 ANSWER 1 OF 2 HCPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2006:1228883 HCPLUS  
DOCUMENT NUMBER: 145:505447  
TITLE: Preparation of high-conductance, calcium-sensitive potassium channel openers  
INVENTOR(S): Imanishi, Yasuhiro; Awai, Nobumasa; Hirai, Miki;  
Hosaka, Toshihiro; Kono, Rikako  
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 164pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006316054	A	20061124	JP 2006-111427	20060414
PRIORITY APPLN. INFO.:			JP 2005-117662	A 20050415
OTHER SOURCE(S):	MARPAT	145:505447		
GI				



AB Title openers, useful for prophylactic and therapeutic treatment of urinary frequency, incontinence, asthma, and chronic obstructive pulmonary disease, are prepared from tricyclic compds. I [ring A = benzene, heterocycle; ring B = benzene, heterocycle, cycloalkane, cycloalkene; ring Q = halo- or (halo)alkyl-substituted pyrazole, isoxazole; R1, R3 = R5R6NCO, R50NR6CO, R5R6NNHCO, R5CO, R5O, R5S, H, etc; R2, R4 = O, cyano, NO<sub>2</sub>, OH, alkoxy, halo, CO<sub>2</sub>H, etc.; R5, R6 = H, (un)substituted alkyl, (condensed) (un)substituted cycloalkyl, (un)substituted heterocyclyl, etc.; m, n = 0-2] are prepared. Thus, deprotection of BOC-protected pyrazole derivative II (R = BOC) gave II (R = H), which inhibited K-induced bladder contraction with IC<sub>50</sub> value of 1-3  $\mu$ M.

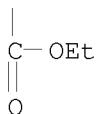
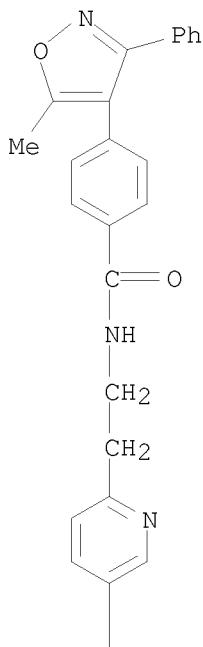
IT 850832-10-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrazoles or isoxazoles as high-conductance, Ca<sup>2+</sup>-sensitive K<sup>+</sup> channel openers for treatment of diseases)

RN 850832-10-9 HCPLUS

CN 3-Pyridinecarboxylic acid, 6-[2-[[4-(5-methyl-3-phenyl-4-isoxazolyl)benzoyl]amino]ethyl]-, ethyl ester (CA INDEX NAME)



L26 ANSWER 2 OF 2 HCPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2005:369275 HCPLUS  
 DOCUMENT NUMBER: 142:430265  
 TITLE: Preparation of substituted pyrazoles and isoxazoles as  
 large conductance Ca-activated K channel openers  
 INVENTOR(S): Imanishi, Yasuhiro; Awai, Nobumasa; Hirai, Miki;  
 Hosaka, Toshihiro; Kono, Rikako  
 PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 224 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005037271	A3	20050901		

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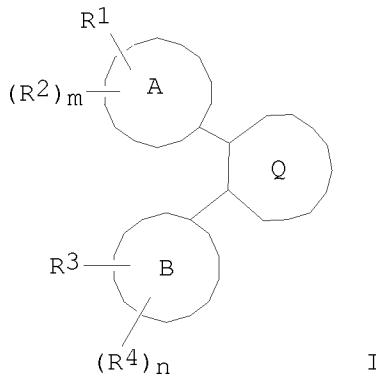
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JP 2007518686 T 20070712 JP 2006-519291 20041015

US 2007060629 A1 20070315 US 2006-574529 20060404

PRIORITY APPLN. INFO.:  
 JP 2003-357325 A 20031017  
 JP 2004-17662 A 20040126  
 JP 2004-85143 A 20040323  
 JP 2004-194172 A 20040630  
 US 2004-584451P P 20040701  
 WO 2004-JP15662 W 20041015

OTHER SOURCE(S): CASREACT 142:430265; MARPAT 142:430265  
 GI



AB Title compds. I [A = benzene, heterocycle; B = benzene, heterocycle, etc.; Q = pyrazolyl, isoxazolyl; R<sub>1</sub>, R<sub>3</sub> = carboxamido, hydrazido, etc.; m, n = 0-2; R<sub>2</sub>, R<sub>4</sub> = oxo, CN, NO<sub>2</sub>, etc.] are prepared. For instance, 4,4,4-trifluoro-1-(4-methylphenyl)butane-1,3-dione is reacted with 3-methylphenylhydrazine•HCl (EtOH, reflux, 20 h) to give 1-(3-methylphenyl)-5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazole (II). Data for over 400 compds. is given. The relaxation effect on K-induced contraction of isolated rabbit urinary bladder and the inhibitory effect on the rhythmic bladder contractions induced by substance P in anesthetized rats is provided for selected example compds. I are useful for the treatment of pollakiuria, urinary incontinence, etc.

IT 850832-10-9P

10540421

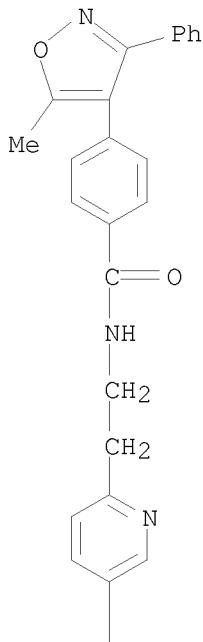
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted pyrazoles and isoxazoles as large conductance Ca-activated K channel openers)

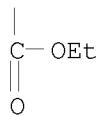
RN 850832-10-9 HCAPLUS

CN 3-Pyridinecarboxylic acid, 6-[2-[[4-(5-methyl-3-phenyl-4-isoxazolyl)benzoyl]amino]ethyl]-, ethyl ester (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



=> file caold  
COST IN U.S. DOLLARS

	SINCE FILE	TOTAL
	ENTRY	SESSION

FULL ESTIMATED COST

13.59 605.70

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE	TOTAL
	ENTRY	SESSION

CA SUBSCRIBER PRICE

-1.60 -6.40

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FILE COVERS 1907-1966  
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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(FILE 'HOME' ENTERED AT 22:11:52 ON 11 MAR 2008)

FILE 'REGISTRY' ENTERED AT 22:11:58 ON 11 MAR 2008

L1 STRUCTURE uploaded  
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L3 2 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 22:14:49 ON 11 MAR 2008

L4 2 S L3  
L5 0 S L4 AND SHINYA, Y?/AU  
L6 2 S L4 AND WATANABE, T?/AU

FILE 'CAOLD' ENTERED AT 22:15:22 ON 11 MAR 2008

L7 0 S L3

FILE 'REGISTRY' ENTERED AT 22:15:28 ON 11 MAR 2008

L8 STRUCTURE uploaded  
L9 0 S L8  
L10 9 S L8 FULL  
L11 9 S L10 NOT L6

FILE 'HCAPLUS' ENTERED AT 22:17:15 ON 11 MAR 2008

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L14 4 S L12 NOT L13  
L15 0 S L14 AND WATANABE, T?/AU  
L16 0 S L14 AND MARUMO, K?/AU  
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L18 2 S L11/USES

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L19 1 S L11

Updated Search

10540421

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SET NOTICE LOGIN DISPLAY

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L23 3 S L21 FULL  
L24 1 S L23 NOT L3  
L25 1 S L24 NOT L11

FILE 'HCAPLUS' ENTERED AT 22:22:31 ON 11 MAR 2008  
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L28 0 S L26 AND WATANABE, T?/AU  
L29 0 S L26 AND MARUMO, K?/AU  
L30 0 S L26 AND KAKEFUDA, A?/AU

FILE 'CAOLD' ENTERED AT 22:23:23 ON 11 MAR 2008

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL  
ENTRY SESSION  
CA SUBSCRIBER PRICE 0.00 -6.40

FILE 'HCAPLUS' ENTERED AT 22:23:39 ON 11 MAR 2008  
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FILE COVERS 1907 - 11 Mar 2008 VOL 148 ISS 11  
FILE LAST UPDATED: 10 Mar 2008 (20080310/ED)

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Updated Search

10540421

substance identification.

=> d his

(FILE 'HOME' ENTERED AT 22:11:52 ON 11 MAR 2008)

FILE 'REGISTRY' ENTERED AT 22:11:58 ON 11 MAR 2008

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L3                   2 S L1 FULL

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L18                  2 S L11/USES

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L19                  1 S L11

FILE 'REGISTRY' ENTERED AT 22:19:57 ON 11 MAR 2008

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FILE 'REGISTRY' ENTERED AT 22:20:39 ON 11 MAR 2008

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L22                  0 S L21  
L23                  3 S L21 FULL  
L24                  1 S L23 NOT L3  
L25                  1 S L24 NOT L11

FILE 'HCAPLUS' ENTERED AT 22:22:31 ON 11 MAR 2008

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10540421

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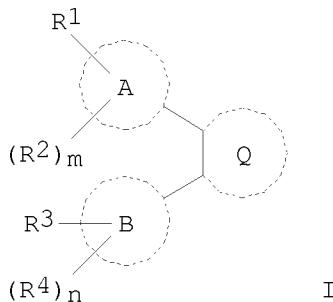
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6920858 USES/RL  
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(L25 (L) USES/RL)

=> d 132, ibib abs hitstr, 1-2

L32 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2006:1228883 HCAPLUS  
DOCUMENT NUMBER: 145:505447  
TITLE: Preparation of high-conductance, calcium-sensitive  
potassium channel openers  
INVENTOR(S): Imanishi, Yasuhiro; Awai, Nobumasa; Hirai, Miki;  
Hosaka, Toshihiro; Kono, Rikako  
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 164pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006316054	A	20061124	JP 2006-111427	20060414
PRIORITY APPLN. INFO.:			JP 2005-117662	A 20050415
OTHER SOURCE(S):	MARPAT	145:505447		
GI				



AB Title openers, useful for prophylactic and therapeutic treatment of urinary frequency, incontinence, asthma, and chronic obstructive pulmonary disease, are prepared from tricyclic compds. I [ring A = benzene, heterocycle; ring B = benzene, heterocycle, cycloalkane, cycloalkene; ring

Q = halo- or (halo)alkyl-substituted pyrazole, isoxazole; R1, R3 = R5R6NCO, R5ONR6CO, R5R6NNHCO, R5CO, R5O, R5S, H, etc; R2, R4 = O, cyano, NO<sub>2</sub>, OH, alkoxy, halo, CO<sub>2</sub>H, etc.; R5, R6 = H, (un)substituted alkyl, (condensed) (un)substituted cycloalkyl, (un)substituted heterocyclyl, etc.; m, n = 0-2] are prepared. Thus, deprotection of BOC-protected pyrazole derivative II (R = BOC) gave II (R = H), which inhibited K-induced bladder contraction with IC<sub>50</sub> value of 1-3  $\mu$ M.

IT 850832-10-9P

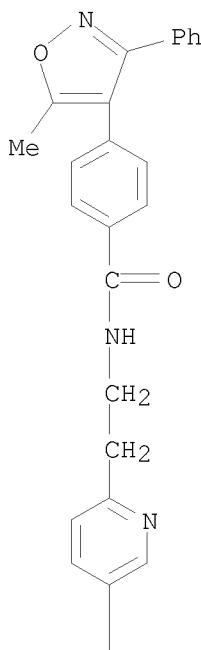
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrazoles or isoxazoles as high-conductance, Ca<sup>2+</sup>-sensitive K<sup>+</sup> channel openers for treatment of diseases)

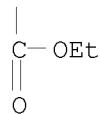
RN 850832-10-9 HCPLUS

CN 3-Pyridinecarboxylic acid, 6-[2-[[4-(5-methyl-3-phenyl-4-isoxazolyl)benzoyl]amino]ethyl]-, ethyl ester (CA INDEX NAME)

PAGE 1-A



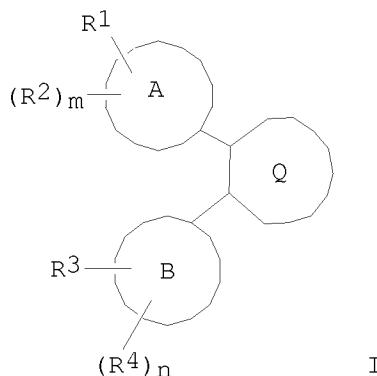
PAGE 2-A



10540421

ACCESSION NUMBER: 2005:369275 HCAPLUS  
DOCUMENT NUMBER: 142:430265  
TITLE: Preparation of substituted pyrazoles and isoxazoles as large conductance Ca-activated K channel openers  
INVENTOR(S): Imanishi, Yasuhiro; Awai, Nobumasa; Hirai, Miki; Hosaka, Toshihiro; Kono, Rikako  
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 224 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

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WO 2005037271	A3	20050901		
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			JP 2004-17662	A 20040126
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			US 2004-584451P	P 20040701
			WO 2004-JP15662	W 20041015
OTHER SOURCE(S):	CASREACT 142:430265; MARPAT 142:430265			
GI				



AB Title compds. I [A = benzene, heterocycle; B = benzene, heterocycle, etc.; Q = pyrazolyl, isoxazolyl; R<sub>1</sub>, R<sub>3</sub> = carboxamido, hydrazido, etc.; m, n = 0-2; R<sub>2</sub>, R<sub>4</sub> = oxo, CN, NO<sub>2</sub>, etc.] are prepared. For instance, 4,4,4-trifluoro-1-(4-methylphenyl)butane-1,3-dione is reacted with 3-methylphenylhydrazine•HCl (EtOH, reflux, 20 h) to give 1-(3-methylphenyl)-5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazole (II). Data for over 400 compds. is given. The relaxation effect on K-induced contraction of isolated rabbit urinary bladder and the inhibitory effect on the rhythmic bladder contractions induced by substance P in anesthetized rats is provided for selected example compds. I are useful for the treatment of pollakiuria, urinary incontinence, etc.

IT 850832-10-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

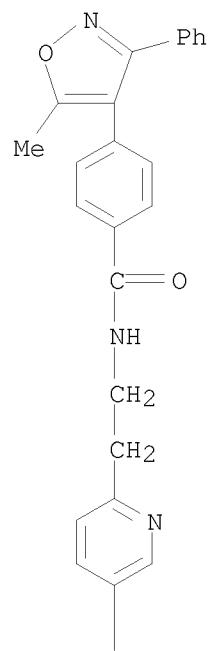
(preparation of substituted pyrazoles and isoxazoles as large conductance Ca-activated K channel openers)

RN 850832-10-9 HCPLUS

CN 3-Pyridinecarboxylic acid, 6-[2-[[4-(5-methyl-3-phenyl-4-isoxazolyl)benzoyl]amino]ethyl]-, ethyl ester (CA INDEX NAME)

10540421

PAGE 1-A



PAGE 2-A

